

AMENDMENTS FO THE SPECIFICATION

Please replace the paragraph on page 9, spanning lines 18-27, with the following amended paragraph:

Fig. 10 The effect of DNA immunization on the survival of mice infected by i.p. injection with HSV-2 in Example 11 is shown. Mice were immunized twice with gD-2 (A) in a two-fold dilution series, or with Δ gB-2 (B) in a half-log dilution series, or with saline. The doses (μ g) are indicated on the figure. The numbers of mice in each group are noted in Table [[9]] 8. Mice were challenged by i.p. injection with 0.25 mL ($10^{5.7}$ pfu) of a clarified stock of HSV-2 strain Curtis, and were observed for three weeks for signs of disease and survival.

Please replace the paragraph on page 45, spanning lines 7-11, with the following amended paragraph:

Table [[7]] 6 shows daily vaginal lesion scores for the experiment. Both the high and low doses of the vaccine caused significant reductions in vaginal lesion severity from days 3 through 15 of the infection compared to the placebo group. The results in Table [[7]] 6 are presented graphically in Figure 9.

Please replace the table heading on page 46, line 1, with the following amended table heading:

TABLE 7 TABLE 6

Please replace the paragraph spanning pages 46-47, lines 31-34 on page 46 and 1-7 on page 47, with the following amended paragraph:

To determine whether mice vaccinated intramuscularly with PNV HSV would produce mucosal HSV-specific antibodies, mice were vaccinated with 12.5 or 1.56 μ g of V1JNS:gD. Vaginal fluid was collected by swab and the antibodies were eluted from the swab using phosphate buffered saline. The eluant was analyzed for the presence of IgG and IgA, specific for HSV-2 protein. The ELISA was performed as described above except that commercially available antibodies specific for mouse IgG (Boehringer) and specific for mouse IgA (Seralab) were used to detect the presence of HSV-specific IgG and IgA in the mouse vaginal samples. The results for IgG are shown in Table [[8]] 7; IgA was not detected in any animal.

Please replace the table labeled "Table 8" on page 47, lines 11-25, with the following amended table:

TABLE 8 TABLE 7

| Animal No. | ELISA Development Time (minutes) | |
|-------------------|----------------------------------|------|
| | 30 | 60 |
| 1031 ^a | <0.1 | <0.1 |
| 1032 ^a | 0.1 | 0.1 |
| 1033 ^a | 0.01 | 0.01 |
| 1035 ^a | <0.1 | 0.1 |
| 1037 ^b | <0.1 | <0.1 |
| 1038 ^b | <0.1 | <0.1 |
| 1039 ^b | <0.1 | <0.1 |
| 1040 ^b | <0.1 | <0.1 |

a - injected with saline immunized once with 12.5 µg V1JNS:gD

b - injected with 1.56 µg V1JNS:gD immunized once with 1.56 ug V1JNS:gD

Please replace the paragraph on page 53, spanning lines 9-21, with the following amended paragraph:

The biological effects of immunization with gD-2 or Δ gB-2 DNA were investigated in separate dose-titration experiments in mice. Animals were immunized by i. m. injection of DNA or were sham-immunized with saline at weeks zero and seven. Sera obtained at week ten were assayed in an HSV-specific ELISA. Table [[9]] 8 shows the seroconversion results and reports the geometric mean titers (GMT) \pm the standard error of the mean (SEM) attained for each dose group. In these assays, pooled sera from the saline-injected control mice were used as the negative controls. The results indicated that injection of each DNA constructions resulted in protein expression *in vivo* and the induction of substantial antibody responses, even at low doses. At the lowest dose tested, 0.8 µg gD-2 DNA, eight of nine immunized mice developed detectable antibody responses.

Please replace the paragraph on page 55, spanning lines 4-23, with the following amended paragraph:

The lethal infection model was useful for confirming the *in vivo* activity of the gD-2 and Δ gB-2 DNA, and for establishing that low DNA doses were effective. However, to more closely

mimic a human disease state, a guinea pig vaginal infection model was used to assay the effects of immunization with a combination of low doses of gD-2 and Δ gB-2 DNA. Seven guinea pigs were immunized with a DNA mixture containing 3 μ g gD-2 DNA and 10 μ g Δ gB-2 DNA at weeks zero and six; fourteen control guinea pigs were sham-immunized with saline. Sera, obtained at nine weeks were analyzed for anti-gD and anti-gB antibodies using antigen-specific ELISAs. Results are shown in Table [[10]] 9. All of the DNA-immunized animals developed ELISA titers to both gD and gB; individual endpoint titers were \geq 300. None of the sham-immunized animals were positive at the lowest dilution (1:30) tested. The results indicated that both DNAs in the mixture were expressed. These sera were also assayed for HSV-2 neutralizing antibodies. Immune sera from all seven DNA-immunized animals were neutralization positive at a 1:10 dilution, six of seven at 1:100, two at 1:1,000, and none at 1:10,000. None of four randomly-selected representative sera from the sham-immunized control animals were positive at dilutions of 1:10 or 1:100.

Please replace the paragraph on page 58, spanning lines 1-2, with the following amended paragraph:

Table [[9.]] 8. Effect of DNA immunization on antibody development in mice

Please replace the table labeled "Table 10" on page 59, spanning lines 1-19, with the following amended table:

Table [[10.]] 9. Effect of immunization with a combination of gD-2 and Δ gB-2
[[Δ gB-2]] DNA on antibody development in guinea pigs.

| immunization | n* | no. positive sera | | \log_{10} ELISA GMT \pm (SEM) | |
|--|----|-------------------|---------|-----------------------------------|-----------------------|
| | | anti-gD | anti-gB | anti-gD | anti-gB |
| gD-2 + [[Δ gB-2]] Δ gB- 2 DNA | 7 | 7 | 7 | 2.62 (.14) | 3.05 (.20) |
| saline | 14 | 0 | 0 | 0.48 (0) [†] | 0.48 (0) [†] |

*number of animals

†For purposes of GMT calculation, sera negative at all dilutions tested were assigned an endpoint titer equal to the reciprocal of the what would have been the next lower dilution had the dilution series been extended; in this case 1:3.